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The discovery of BRCA1 and BRCA2 mutations has enabled physicians to identify individuals at high risk for breast and ovarian carcinoma in hereditary breast-ovarian (HBOC) cancer families. A crucial question pertains to how to use this powerful genetic knowledge for patient benefit, and what detrimental impact on the psychological state and medical behavior it might create. Four hundred and ninety individuals from 32 BRCA1 and 8 BRCA2 families received DNA-based genetic counseling. Five hundred seventy-nine bloodline relatives participated in Georgetown University's psychological portion of the study. Utilization of genetic testing may be highest among persons who have multiple relatives affected with cancer and have health insurance. Individuals who declined to receive their DNA result were eight times more likely than non-carriers to be depressed at 1-month follow-up and germ-line carriers were six times more likely to be depressed at 1-month follow-up. Thirty-nine percent of women who tested positive stated they would consider prophylactic mastectomies and forty-five percent would consider prophylactic oophorectomies. Insurance discrimination remained a concern for individuals who received their test results. We emphasize education of family members in HBOC families, legislative protection of genetic information, and mandatory genetic counseling for individuals who undergo BRCA1/2 testing.

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INTRODUCTION

In 1994 when this study was initiated, two genes, BRCA1 and p53 had been identified and were associated with an extremely high risk for breast cancer. At the time it was hypothesized that at least one other highly penetrant breast cancer susceptibility gene existed. As we come to the close of this study over 300 mutations have been identified in the BRCA1 gene and the "hypothesized second gene", BRCA2, has been found with over 200 different mutations identified to date. It is now predicted that a third BRCA gene exists.

Over the course of this study we have learned that between 5% and 10% of breast cancer cases can be traced to these primary genetic factors. Before the discovery of the *BRCA1* and *BRCA2* genes, the best cancer risk estimate for a first degree relative of a syndrome cancer affected individual in a family with hereditary breast cancer (HBC) or the hereditary breast-ovarian cancer (HBOC) syndrome was 50%. Now the cancer-free members of such families can be divided into mutation carriers and noncarriers by genetic testing. A patient who carries a *BRCA1* or *BRCA2* germ-line mutation has a lifetime breast cancer risk as high as 80-85%, in accordance with the gene's penetrance, while noncarriers have the same risk as the general population. The question posed that led to this study was how to use this powerful genetic knowledge for patient benefit, and what detrimental impact on the psychological state and medical behavior does it have for the patient.

Over the last four years we have identified the following features which appear to be mandatory for the management of hereditary breast cancer at-risk patients: (a) compilation of a detailed

family history of cancer of all anatomic sites; (b) understanding of the natural history of HBC/HBOC and its heterogeneous forms and the pathobiology of hereditary breast cancer; (c) preparation for performance of genetic counseling that is based on the results of DNA sequencing to detect genes related to cancer susceptibility; and (d) necessity for genetic counselors to provide the counselees the information they need to appreciate the emotions they may encounter, such as fear, anxiety, and apprehension, and the potential of being subjected to discrimination by insurance companies and/or employers.

The advantages to the patient as a result of this molecular genetic movement include the following: (a) ability to predict who is and who is not at inordinately high risk for cancer; (b) ability to provide opportunities for highly targeted disease surveillance and management; and (c) the ability to give patients the information they need to make appropriate long-term decisions about matters such as surgical prophylaxis.

Background

Molecular genetic research became highly pertinent to HBC/HBOC when Hall et al.[1] described families with early-onset familial aggregations of breast cancer that were linked to the D17S74 locus on the long arm of chromosome 17. The gene is now referred to as BRCA1. Following this report, Narod et al.[2] studied five large HBOC families from the Creighton University HBC/HBOC resource and found three of them to be positive for linkage to this BRCA1 locus. An international consortium utilizing data from 214 HBC families concluded that 45% of all HBC families without ovarian cancer and nearly all HBC families with ovarian cancer show

linkage to chromosome 17q markers[3]. In 1994, a second susceptibility gene, BRCA2, was mapped to chromosome 13[4] and in 1995 was identified[5].

The availability of this information led to the question of what should be done. Lynch et al.[6] described the use of this information in genetic counseling of high risk family members. Immediate impact of the counseling was assessed and no serious psychological problems were found[6] however, no psychological testing or measures of subsequent adherence to cancer control practices were studied.

For this component, a collaboration with Dr. Caryn Lerman at Georgetown University was instigated for this study. Dr. Lerman has conducted extensive research on the psychological impact of cancer risk notification and adherence to breast cancer screening. In a series of studies, she and her colleagues demonstrated that breast cancer risk notification can produce negative psychological consequences, including anxiety, traumatic stress symptoms, and impairment in daily functioning[7,8]. Moreover, her work has shown that such distress can impair adherence to breast cancer screening[9].

Purpose

The broad goal of this study was to provide genetic counseling to those HBC/HBOC families with identified mutations on BRCA1 and BRCA2 and to assess the psychological and medical impact of counseling. The study is also designed to examine predictors of adverse consequences that could evolve from genetic testing.

BODY

Methods

Figure 1 depicts the process followed by Creighton University in the study. Upon referral of a patient for cancer risk assessment either by self-referral or physician referral, research information and a personal health history and family medical history questionnaire was mailed. Once the individual returned the questionnaire, a working pedigree was constructed and medical information as well as other family participation was solicited. After receiving all available information, a preliminary genetic diagnosis was made as to whether the family appeared to be hereditary, familial, or sporadic. At this point, if the family was found to be hereditary and this was subsequently confirmed based upon all available retrievable information, the adult family members were invited to attend an educational session. This was directed toward the family unit and included intensive education about the natural history, genetics, as well as the implications of DNA disclosure inclusive of the potential for fear, anxiety, apprehension, intrafamily strife, insurance discrimination and even employer discrimination.

At the educational session, DNA was collected on patients who were affected and were first-degree relatives of affected individuals in a HBC and/or HBOC syndrome family. The testing of the DNA was performed in the laboratories of Steven Narod, M.D., of Toronto, Canada, and Gilbert Lenoir, Ph.D., D.V.M., of Lyon, France. This enabled us to have cross checking for accuracy in that the findings were examined in two separate laboratories.

Before genetic test result disclosure at a Family Information Session (FIS), eligible subjects (adult male and female members, ages 18 and older who had at least a 25% probability of having a mutation, and those who did not have a psychiatric or cognitive disorder which precluded providing informed consent) for the psychological portion of the study with Georgetown University were sent an introductory letter that explained the study. The introductory letter was mailed from the Georgetown University Medical Center (GUMC) and included a refusal card for subjects to return if they did not wish to be contacted for the baseline telephone interview. Those who did not return the refusal card within 2 weeks were contacted for the survey. After obtaining oral consent, a 40-minute baseline telephone interview was administered by a professional telephone interviewer at the GUMC using a Computer Assisted Telephone Interviewing (CATI) program. It was emphasized that completing the interview did not obligate them to attend the FIS or to receive BRCA1/2 test results. Variables assessed during the baseline included knowledge about breast cancer genetics, depressive symptoms, cancer-specific distress, role and social functioning, attitudes about the benefits, limitations and risks of genetic testing, BRCA1/2 risk perceptions and testing intentions, personal history of cancer, cancer screening and surgery, and sociodemographic characteristics. At the end of the baseline telephone interview, participants were asked if they were going to attend the group education session and a reply card was mailed from Creighton University to all subjects to confirm their attendance.

At the time of genetic test result disclosure, a FIS was conducted in a geographic area that was convenient to the majority of family members. Each session lasted approximately 1 to 2 hours and was facilitated by an oncologist/geneticist using a semi-structured format after obtaining written informed consent. Topics addressed during the education session included (1) the

inheritance of breast-ovarian cancer susceptibility, (2) cancer risks associated with BRCA1/2 mutations, (3) the benefits, limitations and risks of testing, and (4) assurances of confidentiality of test results and medical information. Following the education session, all participants were given the opportunity to receive their BRCA1/2 test results. Before disclosure, all subjects who decided to receive their test results provided written informed consent and received individual, standardized genetic counseling from an oncologist/geneticist. To increase access to counseling, subjects who had not provided a blood sample before the education session were given the opportunity to be tested at the end of the education session. Test results were made available to these subjects through telephone disclosures or by travel to Creighton University after obtaining written consent and completion of genetic counseling. Structured follow-up assessments of knowledge, psychological distress, cancer surveillance and prophylactic surgery variables were completed at 1-, 6-, and 12-months after genetic testing by a telephone interviewer at the GUMC.

Results

For the most part, our high-risk *BRCA1* and *BRCA2* families have been extremely cooperative, particularly when we have been able to provide them with the convenience of being evaluated in their own geographic area of residence, as evidenced in Table 1 which reflects the geographic sites for our FIS's and educational sessions. In addition to meeting with individuals who are part of a family with an identified BRCA1 or BRCA2 mutation, we were also able to meet with and educate 118 family members who are part of a HBC or HBOC family and are at an increased risk for carrying a BRCA1 or BRCA2 mutation (these individuals were not included in the psychological portion of the study with Georgetown University because a BRCA1 or BRCA2 mutation had not been identified at the time).

Table 2 provides information about the demographic characteristics of the 32 *BRCA1* and 8 *BRCA2* families that have undergone DNA-based genetic counseling. Over the past four years, we have counseled 387 individuals from BRCA1 families and 103 individuals from BRCA2 families. Note that there are fewer positives for *BRCA1* and *BRCA2* mutations than expected based on an autosomal dominant model. Part of the reason for this is that we did test individuals who were judged to be at 25% risk for the germ-line mutation, and thereby this would have reduced the likelihood of showing a 1:1 ratio of positives to negatives for the mutations. The reason for testing individuals at 25% risk included cases where a direct line parent may have died prematurely without cancer and herein we would have estimated that parent had had a 50% risk and thus his or her progeny would have a 25% risk for carrying the germ-line mutation.

Of keen interest, are the number of individuals who were germ-line positive who developed carcinoma of the breast in both the *BRCA1* and *BRCA2* mutation settings. Note also the positive rate for ovarian carcinoma in the *BRCA1* but not the *BRCA2* setting. These findings are important in that we are still learning about the full complement of cancers which may be integral to the *BRCA1* and *BRCA2* phenotypes.

In Table 3 the results reflect the reasons for taking risk assessment in our *BRCA1* and *BRCA2* families. These findings include those from our previous publication dealing with 181 subjects who underwent DNA-based genetic counseling[10]. Note that the major reason for being tested and counseled was concern about the patients' children and primary relatives, with their own personal needs for surveillance being of secondary importance. Their concerns about long-term

planning accounted for about 10% of both *BRCA1* and *BRCA2* of those family members who responded to the question, with a lesser number (7% and 3% respectively) concerned about the implications of prophylactic surgery for themselves. Not unexpectedly, approximately 47% of the patients positive for *BRCA1* and *BRCA2* were not surprised to learn of their results. They stated that so many cancer deaths occurred in their respective families that they thought this would be their own destiny. Thirty-six percent were sad and/or crying when they learned of their results. Those who received what they interpreted as "good news," namely that they did not inherit the germ-line mutation, were both relieved and appeared to be happy.

With respect to the psychological portion of our study, of 900 eligible subjects, 579 (65%) completed the baseline telephone interview, 201 (22%) declined the survey, and 120 (13%) could not be reached for the interview after multiple attempts. Of the 579 active subjects, 40 (7%) withdrew and 7 (1%) expired during the course of the study. In terms of test result uptake, 152 received positive test results, 172 received negative test results, and 225 declined testing. Four subjects received uninformative test results and 26 subjects are waiting for genetic counseling or for mutation analysis to be completed. Of all active subjects, 461 have completed the 1-month follow-up (response rate = 82%), 447 have completed the 6-month follow-up (response rate = 78%), and 424 have completed the 12-month follow-up (response rate = 77%).

RESULTS AND DISCUSSION

Rapid advances in molecular genetics during the past decade have aroused public and professional concern about how cancer risk assessment and DNA testing for cancer susceptibility

can be effectively translated into cancer prevention through targeted screening and management protocols. The application of this knowledge into the clinical practice setting, particularly testing for germ-line mutations in genes such as *BRCA1* and *BRCA2* in hereditary breast cancer (HBC) has become a matter of research priority in oncology[11,12]. However, there are multiple impediments to this application such as the fact that many physicians lack knowledge and appreciation of the significance of genetics in general, and in particular in cancer; family history of cancer is frequently neglected or its significance is not appreciated by health care providers[13,14]; the potential for psychological stress, family disruption, and employment or insurance discrimination has affected patients' willingness and readiness to undergo genetic testing, participate in screening protocols, and consider prophylactic surgery[15,16]. It is essential to provide educational opportunities and to develop mechanisms that will facilitate acquisition of sufficient family history to screen patients for potential genetic risk for cancer and referral for cancer risk assessment and counseling. Insurance executives and public policy makers need to be convinced of the need for privacy of genetic information and the potential economic savings through identification and appropriate management of high-risk individuals.

Table 4 summarizes the major findings that were seen during the genetic counseling of individuals who were tested for BRCA1 or BRCA2. This table represents a cumulative collection of data over the three years with the data in 1998 representing the final number of individuals who were counseled and their responses. Between 1997 and 1998 the number of identified families did not change because no mutations were identified in new families. However, the bloodline relatives did increase significantly between 1997 and 1998 due to new contacts with family members originally not known and new births within families.

As shown in the table, over the three years, the most common reason for seeking test results was out of concern for their children's risk. Surveillance and prevention increased over the past two years as a reason for individuals to receive their result. With regards to prophylactic surgeries, the number of women who would consider prophylactic mastectomy peaked at 54% in 1997, possibly due to an increased number of women who were counseled over that year compared to the number counseled the previous year. Over all, the number of women who would consider prophylactic mastectomy was thirty-nine percent. The number of women who would consider prophylactic oophorectomy peaked at 76% in 1996 and declined to 45% in 1998. A couple of reasons for this decline, a) some women who opted to remove their ovaries before receiving their result, b) the data collected in 1996 included women from BRCA1 identified families only as opposed to 1997/98 which included BRCA2, and c) with the risk for ovarian cancer being less in BRCA2 families, the number of women considering would not be as high as BRCA1. In regards to individuals who were concerned about insurance discrimination, the percentage increased over the three years. This could be due to increased awareness and education of family members regarding the potential of insurance discrimination and possibly due to insurance companies asking specific questions about genetic testing and family histories. Overall, the emotional responses of individuals who received their test result remained unchanged over the three year period. However, the number of individuals who received a negative test result and expressed relief and happiness decreased from 80% in 1996 to 57% and 61% in 1997 and 1998, respectively. The reaction of no surprise for individuals with positive results tended to increase over the three years. The reason for this increase could be due to the fact that over the three years

more women who were already affected with breast and/or ovarian cancer were counseled and by receiving a positive result, confirmed what they already suspected.

The psychological portion of the study completed by Georgetown University over the last four years is best summarized in the following articles:

BRCA1 Testing in Families with Hereditary Breast-Ovarian Cancer[17]**.** Decisions to obtain BRCA1 test results, knowledge and attitudes about genetic testing, and the short-term psychosocial impact of testing were evaluated in 279 subjects who were members of 13 hereditary breast cancer families. Forty-three percent of all eligible subjects received their test results and 57% declined testing; however, 60% of subjects who completed the baseline telephone interview received their BRCA1 test results. Overall, participants were fairly knowledgeable about breast cancer genetics and expected positive outcomes of genetic testing. The average (S.D.) knowledge score was 5.97 (2.91) and participants gave correct responses to 55% of the items. In addition, perceptions of the benefits of genetic testing were significantly higher than perceptions of the limitations and risks of genetic testing ($t=2.71$, $p=.007$). Logistic regression analysis was conducted to identify variables having independent associations with test result uptake. Predictors of test utilization included having health insurance, the number of relatives affected with cancer, knowledge about breast cancer genetics, and perceptions about the benefits of testing. At 1-month follow-up, reductions in depressive symptoms and functional impairment were most pronounced among noncarriers; however, 17% and 33% of unaffected carriers with no prior prophylactic surgery reported intentions to obtain a prophylactic mastectomy and oophorectomy, respectively. These findings suggest that utilization of genetic

testing for BRCA1 mutations may be highest among persons who have multiple relatives affected with cancer and those who have health insurance. In addition, noncarriers may experience the greatest short-term psychological benefits of genetic testing for BRCA1 mutations.

The Influence of Psychological Distress on Use of Genetic Testing for Cancer Risk[18]. The relationships between psychological distress and utilization of genetic testing for BRCA1 mutations were examined in 149 subjects who were members of 11 hereditary breast cancer families. Overall, 58% of respondents received their BRCA1 test results. Bivariate analyses were performed to examine the association between baseline predictor variables, which included global mood distress, cancer-specific distress, cancer risk factors, and sociodemographic characteristics, and utilization of genetic testing. Factors associated with test utilization included gender, objective risk level, and psychological distress. Individuals who received their BRCA1 test results were most likely to be female and have higher objective risk levels, and have moderate to high levels of cancer-specific distress. Hierarchical logistic regression analysis was conducted to evaluate the impact of distress on the use of BRCA1 testing. In the final model, there were significant main effects for age, gender, objective risk level, and cancer-specific distress. Females were almost three times as likely as males to receive their test results (O.R.=2.7; 95% C.I.= [1.2,6.1]) and those with an elevated objective risk were five times as likely to receive their test results (O.R.=5.5; 95% C.I.=[2.5,11.9]). In addition, individuals who had moderate to high levels of cancer-specific distress were almost three times as likely as those with low levels of distress to receive their test results (O.R.=2.9; 95% C.I.=[1.3,6.5]). These findings suggest that cancer-specific distress may motivate utilization of BRCA1 testing.

What You Don't Know Can Hurt You: Adverse Psychological Effects in Members of BRCA1 and BRCA2-linked Families Who Decline Genetic Testing[19]. The long term psychological impact of genetic testing for BRCA1 and BRCA2 mutations was evaluated in 327 male and female members of 33 hereditary breast cancer families who were identified as carriers, noncarriers, or decliners of genetic testing. In Figure 2, the average baseline distress score was 7.8±0.4. Subjects who had high levels of cancer-related distress at baseline and declined genetic testing exhibited increases in depression at the 1- and 6-month follow-ups while depression rates among noncarriers decreased and stayed the same among carriers. Specifically, among subjects who declined genetic testing, depression rates increased from 26% at baseline to 47% at 1-month. Stratified logistic regression analysis, controlling for baseline depression and other confounding variables, was performed to evaluate the effects of study group on depression at follow-up. Within the high stress group, decliners were eight times more likely than noncarriers to be depressed at 1-month follow-up (O.R.=8.0; 95% C.I.=[1.9,33.5]) and carriers were six times more likely than noncarriers to be depressed at 1-month follow-up (O.R.=6.1; 95% C.I.=[1.7,21.9]). At 6-month follow-up, rates of depression were significantly higher among decliners. Forty-one percent of decliners were depressed at 6-month compared to 32% of carriers and 18% of noncarriers (χ^2=4.2, p=.04). These findings suggest that the presence of cancer-related stress symptoms at baseline is predictive of long term adverse psychological reactions among individuals who decline genetic testing. Individuals who decline genetic testing may benefit from education and counseling even though they do not receive test results and should be monitored for adverse psychological effects.

Communication of BRCA1/2 Test Results in Hereditary Breast Cancer Families[20].

Communication of BRCA1 and BRCA2 test results to first-degree relatives was evaluated one month following test result disclosure in 80 carriers and 83 non-carriers. Overall, carriers and non-carriers were most likely to communicate their test results to a sister and were least likely to communicate their test results to an offspring under age 18. Different factors were associated with communication to relatives among carriers and non-carriers. Among carriers, females were significantly more likely than males to communicate their test results to a sister and an offspring under age 18. Carriers who had a personal history of cancer and who were 50 and older were also more likely to have communicated their test results to an adult child. Among noncarriers, those who had a higher perceived risk of having a BRCA1/2 mutation were significantly more likely to communicate their test results to a brother and an adolescent child. These findings suggest that both carriers and non-carriers are likely to discuss their BRCA1/2 test results with siblings and adult children, but are reluctant to communicate their test results to adolescent children under age 18. In addition, reasons for discussing genetic test results with relatives may vary among carriers and non-carriers.

Concurrent with this information that we have learned through the course of the last four years, we have brought our expertise in cancer genetics to numerous successful collaborations which have advanced the field. These studies have included discoveries of genetic linkage in certain cancer prone families[21,22-24], identification of cancer-associated mutations[25,26], new phenotypic features of previously described hereditary cancer syndromes[27], studies of screening and prophylactic surgery in high-risk patients[28,29], pathology correlates of hereditary cancer syndromes[30-34], and tumor genetics[35,36].

Limitations of our study included the fact that data collection was done during the time of genetic test disclosure and individuals' emotional needs took precedence over data collection, therefore, not all questions were asked of all individuals; three genetic counselors provided results to individuals and their differing styles may have influenced data collection; not all individuals counseled agreed to participate in Georgetown's psychological portion of the study.

Our recommendations continue to be more education of family members who are part of a hereditary breast/ovarian cancer family and are at an increased risk for harboring one of the deleterious mutations. A strong voice for legislative protection of genetic information is a must for individuals who choose to undergo testing and subsequently receive their result so that they may be fully aware of their risk for developing breast and/or ovarian cancer and proceed with appropriate screening measures. In addition, we continue to support that psychological counseling is a must for individuals who are at an increased risk for developing breast and/or ovarian cancer and who may choose to undergo genetic testing of the BRCA1 and BRCA2 genetic mutations.

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Figure 1

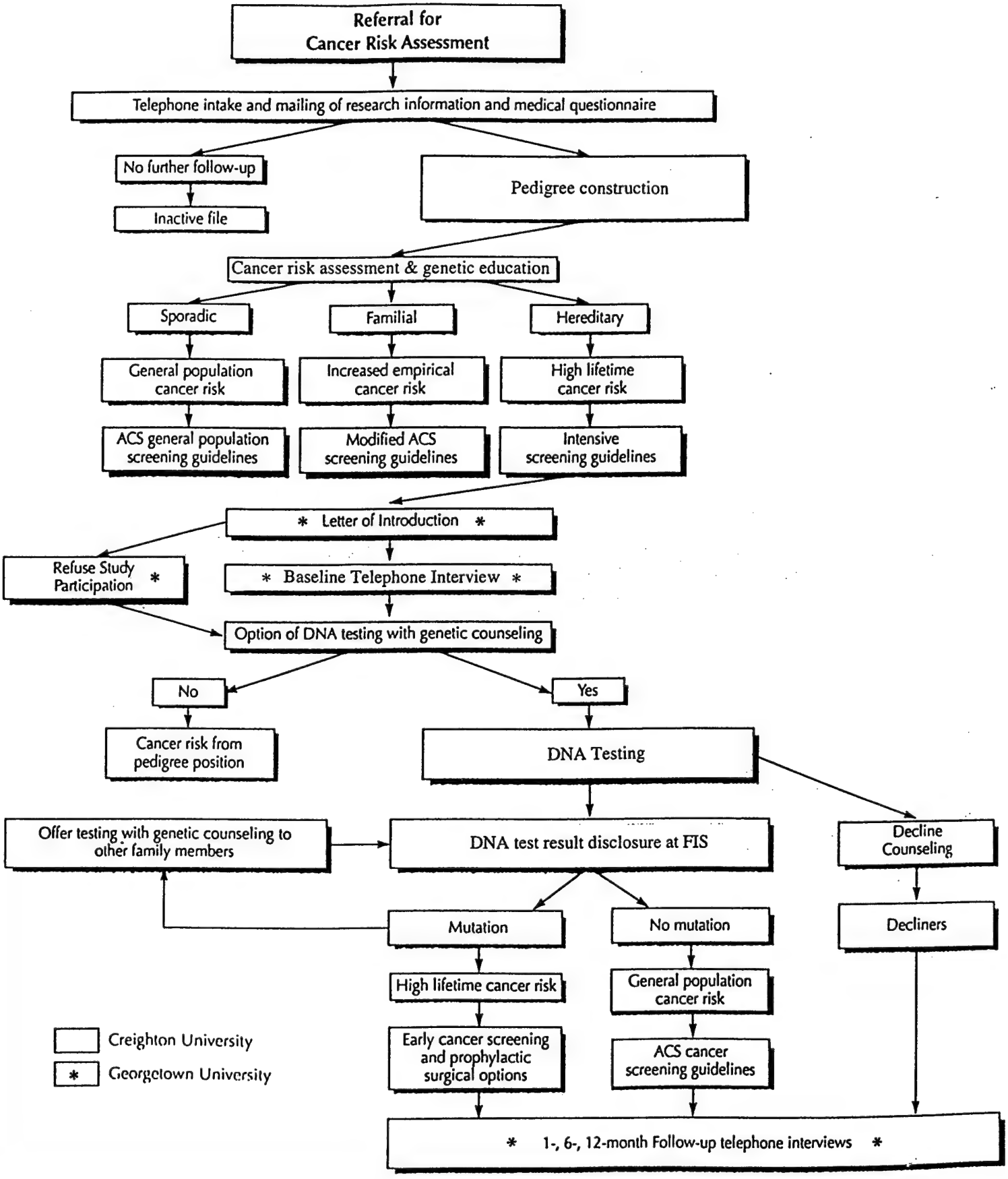

Referral for Cancer Risk Assessment
Telephone intake and mailing of research information and medical questionnaire
No further follow-up
Inactive file
Pedigree construction
Cancer risk assessment & genetic education
Sporadic
Familial
Hereditary
General population cancer risk
Increased empirical cancer risk
High lifetime cancer risk
ACS general population screening guidelines
Modified ACS screening guidelines
Intensive screening guidelines
* Letter of Introduction *
Refuse Study Participation *
* Baseline Telephone Interview *
Option of DNA testing with genetic counseling
No
Yes
Cancer risk from pedigree position
DNA Testing
Offer testing with genetic counseling to other family members
DNA test result disclosure at FIS
Decline Counseling
Mutation
No mutation
Decliners
High lifetime cancer risk
General population cancer risk
Early cancer screening and prophylactic surgical options
ACS cancer screening guidelines
Creighton University
* Georgetown University
* 1-, 6-, 12-month Follow-up telephone interviews *

TABLE 1

COUNSELED INDIVIDUALS

FAMILY	DATE OF FIS	LOCATION
BRCA1		
2979	8-29-93	OMAHA, NE
1816	3-7-92 & 8-19-95	MINNEAPOLIS, MN
2775	7-9-94	IOWA CITY, IA
1234	8-20-94	OMAHA, NE
1813	1-29-95	SIOUX CITY, IA
2090	2-18-95	KANSAS CITY, KS
2770	3-18-95	KANSAS CITY, KS
2651	4-22-95	TOPEKA, KS
1973	5-27-95	OMAHA, NE
2944	5-27-95	KANSAS CITY, KS
3079	6-10-95	QUEENS, NY
1086	10-7-95	MINNEAPOLIS, MN
2749	10-28-95	MOLINE, IL
1252	10-29-95	MOLINE, IL
2850	3-13-96	SPOKANE, WA
BRCA2		
2932	1-13-96	ST. LOUIS, MO
3433	5-11-96	FARGO, ND
	7-20-96	SEATTLE, WA

SESSIONS THAT MULTIPLE FAMILIES WERE INVITED TO BASED ON GEOGRAPHIC LOCATION

	BRCA1/2		HBC/HBOC
8-24-96	KANSAS CITY, KS	5-1-98	LANSING, MI
9-8-96	BALTIMORE, MD	5-2-98	LIMA, OH
9-28-96	OMAHA, NE	5-3-98	TOLEDO, OH
10-19-96	RICHMOND, VA	5-8-98	HIGH POINT, NC
11-9-96	TULSA, OK	5-9-98	CHARLOTTE, NC
11-10-96	DALLAS, TX	5-15-98	HARRISBURG, PA
2-15-97	LOS ANGELES, CA	5-16-98	SYRACUSE, NY
3-1-97	ORLANDO, FL	5-28-98	VIPER, KY
3-2-97	TALLAHASSEE, FL	6-3-98	TOPEKA, KS
3-22-97	SEATTLE, WA	6-14-98	CHICAGO, IL
4-26-97	MINNEAPOLIS, MN	6-17-98	OMAHA, NE
5-17-97	DES MOINES, IA	6-26-98	FARGO, ND
5-31-97	LOUISVILLE, KY	6-27-98	MINNEAPOLIS, MN
6-1-97	LANSING, MI	7-18-98	SAN FRANCISCO, CA
6-28-97	NEW YORK, NY	7-19-98	DENVER, CO
6-29-97	PHILADELPHIA, PA	7-24-98	GREAT FALLS, MT
		7-25-98	SEATTLE, WA
		7-26-98	PORTLAND, OR

TABLE 2. DEMOGRAPHIC CHARACTERISTICS OF 32 BRCA1 FAMILIES AND 8 BRCA2 FAMILIES.

	BRCA1	BRCA2
Total number of family members:	6662	1914
Total number of blood relatives:	4295	1081
Total number of family members educated about HBOC and the role of genetic testing:	450	119
Adults who are not blood relatives	75	24
Number of family members (of direct lineage >18 y.o.a.) who donated a DNA sampled:	**697**	**183**
Gene positive:	268	81
Gene negative:	399	94
Pending:	24	8
Ambiguous:	6	0
Total number counseled and given gene status:	**387**	**103**
Gene positive:	162	48
Gene negative:	222	55
Ambiguous:	3	0

Total number of cancer cases:	**537**	**166**

Top four cancer sites for BRCA1:

1. Breast	238
Positive	118
Negative	13
Gene status unknown	107
2. Ovarian	91
Positive	23
Negative	3
Gene status unknown	65
3. Colorectal	33
Positive	7
Negative	4
Gene status unknown	22
4. Cervical	19
Positive	0
Negative	7
Gene status unknown	12

Top four cancer sites for BRCA2:

1. Breast	89
Positive	35
Negative	3
Gene Status Unknown	51
2. Lung	16
Positive	0
Negative	2
Gene status unknown	14
3. Prostate	14
Positive	5
Negative	0
Gene status unknown	9
4. Ovarian	7
Positive	0
Negative	0
Gene status unknown	7

TABLE 3. DEMOGRAPHIC CHARACTERISTICS AND REASONS FOR SEEKING RISK ASSESSMENT IN 387 COUNSELED MEMBERS OF 32 BRCA1 FAMILIES AND 103 COUNSELED MEMBERS OF 8 BRCA2 FAMILIES.

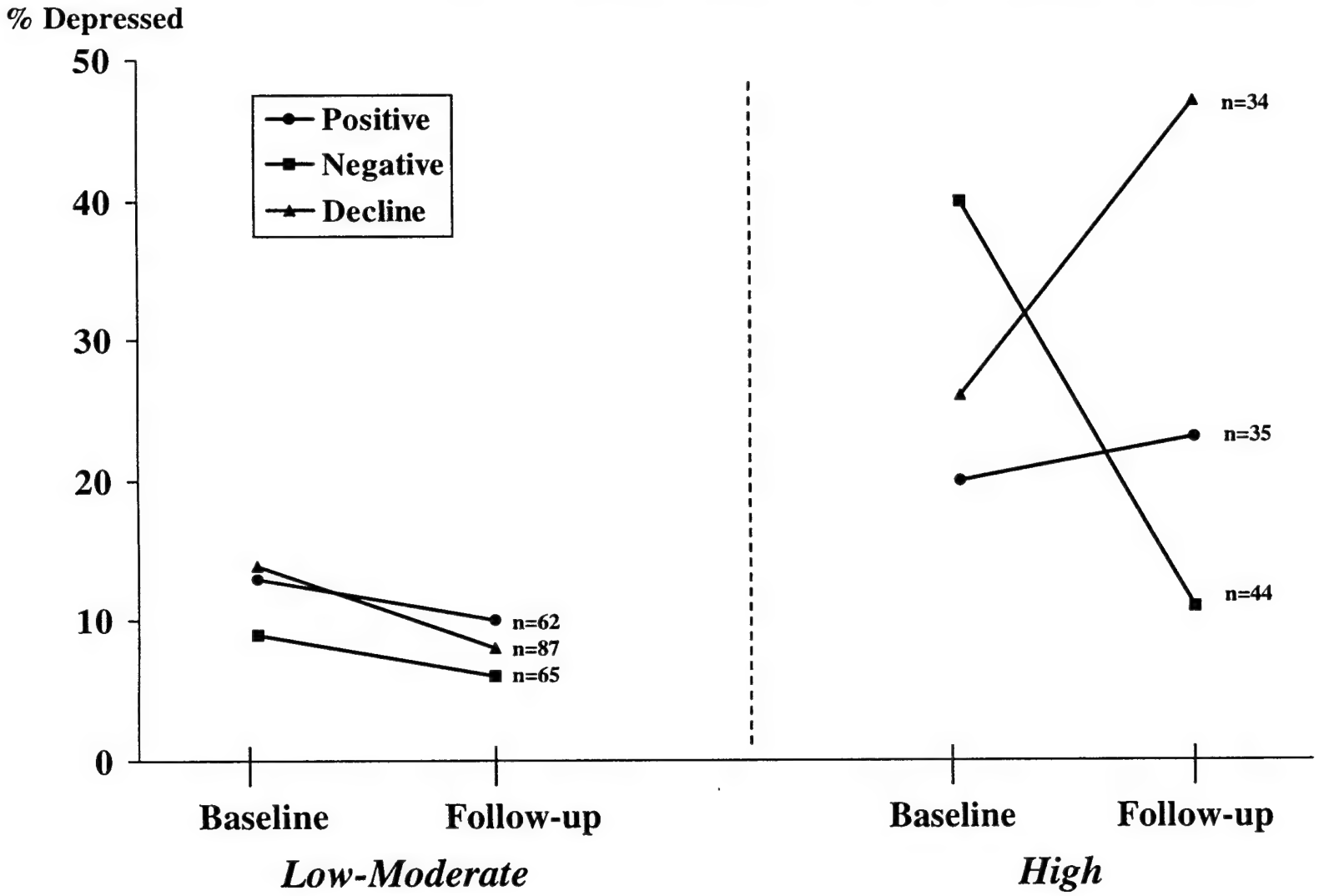
	Counseled BRCA1 Individuals	Counseled BRCA2 Individuals
Sex	Number	Number
Male	101	29
Female	286	74
BRCA1 Cancer Affected	**86**	**21**
Age at Time of Counseling, years		
Mean	45	44
Range	19-84	19-78
Reason for seeking risk assessment		
Children and/or family	204/370	56/103
Surveillance	145/370	50/103
What future holds	37/370	10/103
For possible prophylactic surgery	25/370	3/103
Relieve anxiety	16/370	6/103
Family pressure	4/370	2/103
Emotional Response to receiving results		
Gene positive		
Surprised	11/155	0/48
Appeared not to be surprised	73/155	28/48
Appeared to be sad/crying	56/155	16/48
No apparent reaction	31/155	7/48
Claimed to feel guilty	10/155	0/48
Claimed a sense of relief	9/155	2/48
Appeared to be angry	5/155	0/48
Happy	1/155	0/48
Gene negative		
Appeared to be happy	139/208	42/55
Appeared to be relieved	114/208	24/55
Appeared to be surprised	42/208	18/55
No apparent reaction	12/208	2/55
Claimed feelings of survival guilt	4/208	2/55
No surprise	8/208	2/55
Sad/Crying	24/208	7/55
Angry	0/208	0/55

* Not all individuals were asked the questions or responded to the questions when asked by the counselor.

Table 4. CUMULATIVE DATA ON FAMILIES WHO PARTICIPATED IN BRCA1 & BRCA2 TESTING AND GENETIC COUNSELING

	1996	1997	1998
Number of BRCA1 & BRCA2 Families	14	37	37
Bloodline Relatives	2549	4698	5376
Number of Individuals Who Underwent DNA Testing	388	855	880
Number of Individuals Who Received Their DNA Test Result	181	424	490
Positive Result	78	179	210
Negative Result	100	241	277
Ambiguous Result	3	4	3
Top Two Reasons for Seeking DNA Test Result			
Concern for Children	56%	54%	55%
Surveillance/Prevention	30%	41%	41%
Number of BRCA1 or BRCA2 Positive Women who would Consider Prophylactic Mastectomy	35%	54%	39%
Number of BRCA1 or BRCA2 Positive Women who would Consider Prophylactic Oophorectomy	76%	64%	45%
Number of Individuals who were Concerned About Insurance Discrimination	25%	43%	45%
Most Common Emotional Response of Individuals who Tested Negative			
Relieved and/or Happy	80%	57%	61%
Most Common Emotional Responses of Individuals who Tested Positive			
Not Surprised	27%	45%	50%
Sad, Angry, and/or Guilty	19%	34%	20%

Figure 2. Depression Rates by BRCA1/2 Test Result, Baseline Stress, and Time



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